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Assessment of some Immunological and biochemical parameters in diabetic type 2 patients suffered of Covid-19

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ABSTRACT

COVID-19 caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has threatened every civilian as a global pandemic. The immune system poses the critical interactive chain between the human body and the virus. The current study aimed to assessment whether comorbidity with type 2 diabetes (T2D) affects the immunological response in COVID-19 patients. This case-control study (comparative) was carried out in Baghdad Al-karkh hospitals/ isolation units for Patients covid-19, which included 90 subjects from November 2021 to the end of April 2022, as of which 30 participants were with T2D patients, 30 were T2D patients suffer of covid-19, with positive RT-PCR for covid-19 and the remaining 30 were nondiabetic (NDM) of aged (50-85) years. To study concentrations of Interleukin 6(IL-6), Interleukin 2 Receptor Beta (IL-2R β), Procalcitonin (PCT), Ferritin, D-dimer, HbA1c, blood urea(BU), and serum creatinine . The current study showed a significant increase in IL-6 (362.4±60.01pg/ml), IL-2R β (8.8±2.7%), PCT (205±25.7mg/dl), Ferritin(), D-dimer(), HbA1c(), blood urea(58±12.7mg/dl), and serum creatinine (1.1±0.2mg/dl) in T2D with COVID-19 patients compared to the control group (222.8±30.7pg/ml, 4.6±1.3%, 99±15.1mg/dl, 35±9.6mg/dl, 0.65±0.03mg/dl respectively, at the probability value ($P<0.05$). The COVID-19 patients comorbid with T2D demonstrated distinguishable immunological parameters, which represented clinical relevancies with the predisposed disease severity in T2D.

Keywords: *COVID-19; T2D; D-dimer; Procalcitonin.*

INTRODUCTION

From January, 2020, we have been facing an unprecedented outbreak of coronavirus infectious disease-19 (COVID-19), which is now threatening every civilian in the world [1]. COVID-19 is caused by a novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) [2, 3]. Although COVID-19 leads to mild flu-like symptoms in the majority of affected patients, the disease may cause severe or even frequently lethal complications such as acute respiratory distress syndrome (ARDS) and multiorgan dysfunction (MODS) [1, 2, 4, 5]. And the coronavirus, including SARSCoV-2, may likely pose a continuous threat to human health in the future [6].

The incidence of type 2 diabetes mellitus (T2D) is increasing worldwide, and diabetes is one of the leading causes of morbidity and mortality globally among chronic diseases [7, 8]. T2D is well established with alterations in both adaptive and innate immune systems, thus increasing the risk of susceptibility to most kinds of infections [9, 10]. Up to now, T2D is one of the most important comorbidities linked to the severity of all three known human pathogenic coronavirus infections, including SARS-CoV-2 [2, 10–12].

Among chronic comorbidities of COVID-19, diabetes had the second highest incidence rate (7.4%–19.0%), following hypertension (15%–30%). Patients with diabetes were likely at higher risk for severe COVID-19 and mortality [13,14]. The IL-6, ferritin, C-reaction protein, and D-dimer levels were significantly increased in patients with diabetes, suggesting that a marked inflammatory cytokine storm was associated with a more pejorative prognosis compared to patients without diabetes [15]. To date, the detailed effect of diabetes or hyperglycaemia on the immune cells and immune system in patients with COVID-19 remains unclear.

COVID-19 infection can trigger a ‘cytokine storm’, which refers to the massive release of pro-inflammatory cytokines that contribute to acute lung injury and unfavourable prognosis[16,17]. Common laboratory findings of the virus include lymphocytopenia; neutrophilia; elevated levels of lactate dehydrogenase; C-reactive protein (CRP); D-dimer; IL (interleukin)-2, IL-6 and IL-10; and reduced levels of CD8 + T cells, in particular, as well as decreased CD4+ T cells, and natural killer (NK) cells [18,19]. The immune response to SARS-CoV-2 infection can cause tissue damage in the liver, kidneys, heart and lungs, and may account for the relationship between elevated pro- inflammatory cytokines and the most severe clinical manifestations of COVID-19[20–22].

MATERIALS AND METHODS

This was a case-control study (comparative) of hospitalized patients admitted to the Baghdad Al-karkh hospitals/ isolation units, from November 2021 to the end of April 2022. as of which 30 participants were with T2D patients, 30 were T2D patients suffer of covid-19, with positive RT-PCR for covid-19 and the remaining 30 were nondiabetic (NDM) of aged (50-85) years. All participants enrolled were confirmed cases of COVID-19 diagnosed in compliance with the Guidelines for Diagnosis and Management of COVID-19 (6th edition) issued by the National Health Committee of China. Respiratory specimens were collected and then shipped to designated authoritative laboratories to detect the SARSCoV-2 as previously reported [1, 5].

Blood samples were collected from patients, and analysis was conducted to estimate the concentration of preptin using Enzyme Linked. Immunosorbent Assay (ELISA) Sunlong Biotech Company kits with the sandwich method [11], Hba1c by using AFIAS-1/6, and biochemical tests includes : fasting blood glucose (RBS) measured by enzymatic oxidation method in the presence of glucose oxidase, blood urea (BU) by using Colorimetric and enzymatic method (Urease), and serum creatinine by usingJaffe method, colorimetric reaction.

Briefly, continuous parameters were presented as the mean ± SD or median according to data distribution. The statistical difference between two groups was determined by nonpaired Student’s t-test unless the data were not normally distributed d, in which case Mann-Whitney’s U test was used instead. The chi-squared goodness-of-fit (Fisher’s exact) test was used for the comparison of incident rates and proportions for categorical variables. SPSS18.0 or GraphPad Prism 5.0 was used to perform all tests and generate values. A p value of less than 0.05 was considered statistically significant.

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RESULTS

The results showed a significant increase in concentrations of biochemical parameters include Glucose (mg/dL), Urea (mg/dL), Creatinin (mg/dL), Ferritin (ng/mL), HbA1c (%)and D-dimer (ng/mL) in T2D withcovid-19 group compared to the control group at the probability (P<0.05), as shown in Table (1) as illustrated in Figures (1,5,6,7,8 and 9) respectively; While the immunological parameters showed significant increase in concentrations of IL-6(pg/mL) and PCT (pg/mL) as in table (2) and figures (2 and 3). The concentration of IL-2Rβ(pg/mL) showed significant decrease as illustrated in table (2) and figure (4).

TABLE 1: Concentrations of biochemical Parameters in T2D withcovid-19 group and T2D without covid-19 group compared to the control group.

Parameters	T2D withcovid-19 group		T2D without covid-19 group		control group		P value
	M	SD	M	SD	SD	M	
Glucose (mg/dL)	284..4	70.41	291.8	45.34	96.88	5.953	0.0001<
Urea (mg/dL)	67.54	42.63	35.85	15.13	17.76	2.378	0.0001<
Creatinin (mg/dL)	1.052	0.5185	1.482	1.452	0.7017	0.4477	0.0074<
Ferritin (ng/mL)	557.3	290	267.5	70.29	154.2	42.31	0.0001<
HbA1c (%)	8.170	1.179	7.077	0.6005	6.331	0.4501	0.0001<
D-dimer (ng/mL)	3.939	2.799	0.9112	0.3044	0.3283	0.1524	0.0001<

TABLE 2: Concentrations of Immunological Parameters in T2D withcovid-19 group and T2D without covid-19 group compared to the control group.

Parameters	T2D withcovid-19 group		T2D without covid-19 group		control group		P Value
	M	SD	M	SD	M	SD	
IL-6(pg/mL)	14.39	4.078	12.89	5.955	10.02	2.720	0.0012<
IL-2Rβ(pg/mL)	74.19	30.91	82.25	31.21	130.0	58.16	0.0001<
PCT (pg/mL)	22.89	15.79	15.73	2.908	11.59	4.119	0.0001<

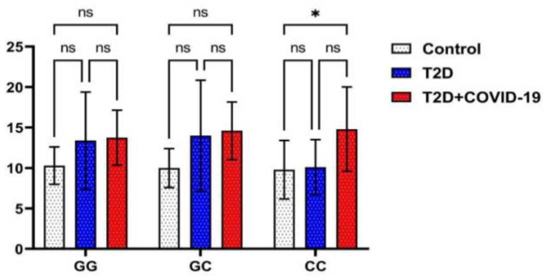

Fig. (1): Concentration of IL-6 (pg/ml) in T2D withcovid-19 group and T2D without covid-19 group compared to the control group.

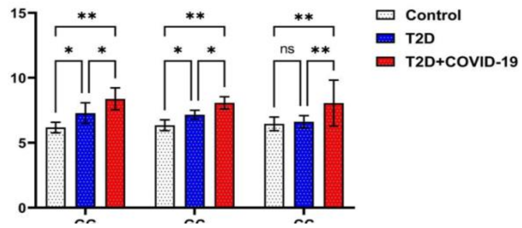

Fig. (2): Concentration of Hba1c (%) in T2D withcovid-19 group and T2D without covid-19 group compared to the control group.

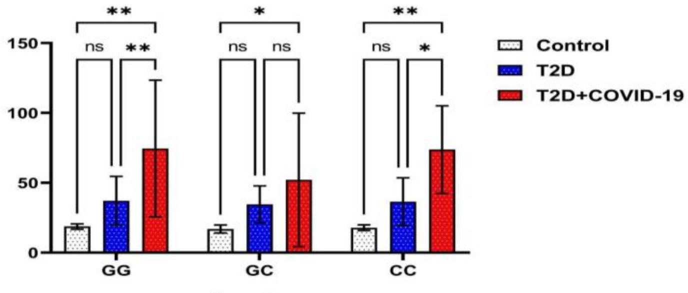

Fig. (3): Concentration of PCT (pg/ml) in T2D withcovid-19 group and T2D without covid-19 group compared to the control group.

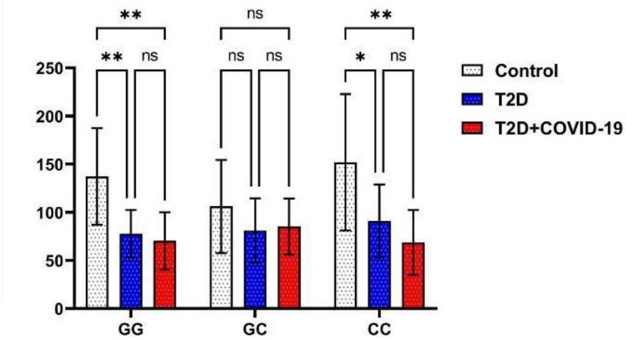

Fig. (4): Concentration of IL2-Rβ (pg/ml) in T2D withcovid-19 group and T2D without covid-19 group compared to the control group.

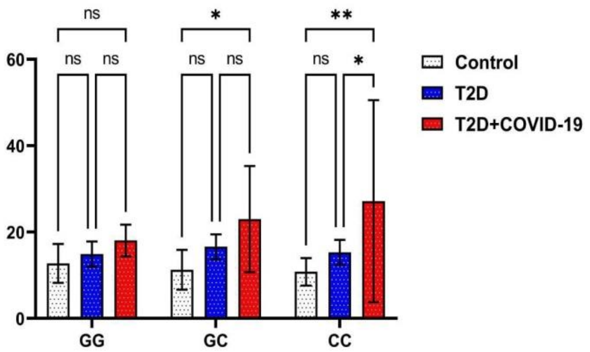

Fig. (5): Concentration of Ferritin (ng/mL) in T2D withcovid-19 group and T2D without covid-19 group compared to the control group.

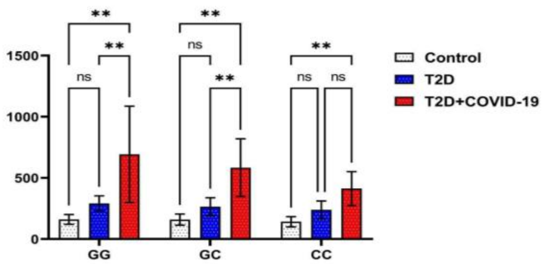

Fig. (6): Concentration of Glucose (mg/dL) in T2D withcovid-19 group and T2D without covid-19 group compared to the control group.

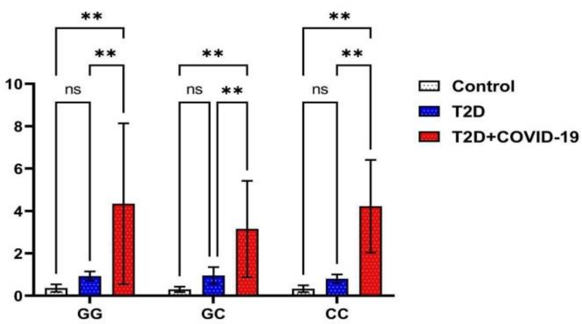

Fig. (7): Concentration of D-dimer (ng/mL) in T2D withcovid-19 group and T2D without covid-19 group compared to the control group.

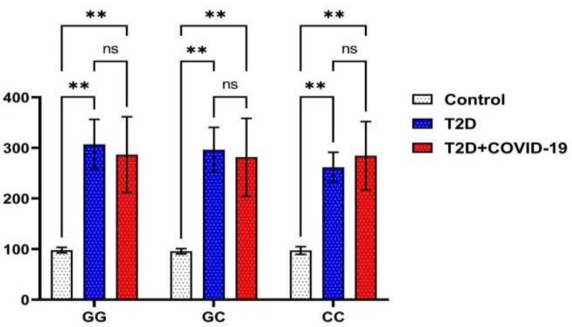

Fig. (8): Concentration of Creatinine (mg/dL) in T2D withcovid-19 group and T2D without covid-19 group compared to the control group.

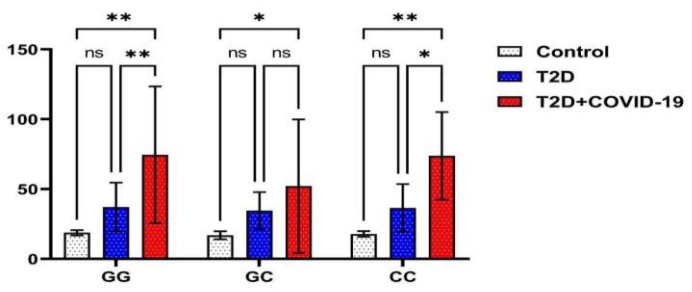

Fig. (9): Concentration of Urea (mg/dL) in T2D withcovid-19 group and T2D without covid-19 group compared to the control group.

DISCUSSION

The ongoing pandemic of COVID-19 is now a global healththreatening crisis [22, 23]. Within the past half year, we have accumulated limited knowledge of the novel infectious disease. The immune response is believed to be most involved in the pathological process of COVID-19 [24-25]. The effectual host immune response including innate and adaptive immunity against SARS-CoV-2 is crucial to control and resolve the viral infection [26, 25]. However, the severity and outcome of COVID-19 might also be associated with dysregulated immune response and excessive production of proinflammatory cytokines [22, 23]. The immune system is impaired during the disease, characterized by leukocytopenia (esp. lymphocytopenia) and uncontrolled systemic inflammatory response in the severe cases [27].

To the best of our knowledge, Th2 cells typically produce IL4, IL-6, Il-8, IL-10, and IL-13, whereas cytokines, such as IL-1b, IL-2R, and TNF-a, belong to the Th1 cell response. As two extremes on a scale, Th1 and Th2 responses play different roles and may contribute to immunopathology. Distinct from Th1 cell pro-inflammatory function and antiviral response by stimulating macrophages and cell-mediated immunity, Th2 cells tend to oppose the inflammatory reaction and promote antibody response and inhibit Th1 cell-induced antiviral function[28].

D-dimer was measured in five studies [articles 29, 30, 31–33]. High D-dimer levels were reported in both severe and mild patients, and those with comorbidities including diabetic patients, patients who developed ARDS and a post-kidney transplant patient. Neutrophilia, increased D-dimer and IL-6 were associated with COVID-19 patients with ARDS who progressed to death [32,33].

IL2Rβ chain common to IL-2 and IL-15, on CD8+ T cells during chronic viral infection in both humans and mice[34].

CONCLUSION

Our study provides distinct evidence that T2DM or hyperglycaemia patients showed an obvious decrease in immune cells and imbalance of TH1/Th2 cytokines, which were associated with the high mortality of COVID-19 patients with T2DM.

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